Ectopy in Trauma Patients: Cautions for Use of Heart Period Variability in Medical Monitoring

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Introduction: Heart period variability measurements have been proposed for use in early prediction of mortality or the requirement for life-saving interventions in trauma patients. However, the presence of even one ectopic beat (EB) and/or electromechanical noise compromises the accurate calculation of heart period variability. We tested the hypothesis that ECGs from trauma patients exhibit a greater frequency of EBs than healthy human research subjects. **Methods:** Continuous ECGs were recorded in 20 healthy human subjects at rest, 108 healthy human subjects undergoing experimentally induced progressive central hypovolemia (via lower body negative pressure, LBNP), and 245 trauma patients. The proportions of subjects/patients with at least one EB were identified in each group. **Results:** ECG waveforms from 20% and 18% of healthy human subjects at rest or undergoing LBNP, respectively, contained at least one EB. ECG waveforms from 36% of the trauma patients were found to contain either EBs (35%) or electromechanical noise (1%). **Conclusions:** A significant number of EBs occur in healthy subjects both at rest and during progressive reduction in central blood volume, and trauma is associated with a near doubling of this incidence. As both EBs and noise result in invalid heart period variability calculations, these metrics as currently calculated could not be used in approximately 36% of trauma patients. The limited use in nearly two of every five trauma patients indicate that it is unlikely that continuous heart period variability measurements could substantially improve pre-hospital or emergency room decision-support in trauma.
Keywords: physiologic monitoring, heart rate variability, heart rate complexity, hypovolemia.

DURING MISSION PERFORMANCE in dangerous environments, it would be desirable to have personnel wear a remote monitoring system that could transmit information about the individual's physiological status to medical personnel that may not have physical access to the individual. This concept of continuous, remote, physiological monitoring has gained traction for use in soldiers (15), astronauts (10), and emergency first responders (8) and implementation systems have been actively pursued by military developers (11). The military system as currently envisioned contains ECG measurement as an integral component, with the intent that analysis of the ECG waveform could provide valuable information as to physiological status, particularly in the case of traumatic injury. In addition to remote triage systems, ECG is a component on all medical monitoring systems currently used in pre-hospital, aeromedical evacuation, and in-hospital settings and there is a great interest in the ability of ECG-derived metrics to predict patient outcome (12,16).

In this regard, measurements of heart period variability have been proposed for use in early prediction of

mortality (1,5–7) and the requirement for life-saving interventions (4) in trauma patients. We have been interested in determining whether these metrics, derived from a simple ECG, would provide additional information about the status of trauma patients in pre-hospital settings such as during battlefield missions (i.e., remote triage), medical air evacuation from the battlefield, or civilian point of injury (5,15). However, the presence of at least one ectopic beat (EB) or electromechanical noise compromises the accurate calculation of heart period variability (3,20). Furthermore, many of these metrics require extended ECG waveforms of up to 800 beats, increasing the probability of the ECG containing EBs and/or noise (1).

A number of studies have shown that even healthy human subjects exhibit EBs (14). It has been reported that 1% of clinically normal people exhibit EBs based on short-term ECG testing, but this increases to 40–75% of healthy individuals when tested with 24–48-h ambulatory ECG monitoring (14). Since the proportion of trauma patients who exhibit EBs is unknown, it is unclear how many false positives or false negatives might result from the use of heart period variability monitoring due to the effect of EBs on these calculations. This determination is essential before proposing the use of heart period variability metrics in any patient population in which EBs might be increased, either as a result of physiological status or pharmacological interventions.

Since the requirement for noise-free and ectopy-free, continuous ECG waveforms may limit the practical utility of heart period variability measurements for the purpose of patient monitoring and diagnostics, we conducted a review of ECG waveforms obtained from healthy human subjects and pre-hospital trauma patients to further elucidate the incidence of EBs in these populations. We hypothesized that ECGs from trauma

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patients would exhibit a greater frequency of EBs than healthy human research subjects.

METHODS

Data were collected from two protocols. Each protocol was approved by both the Institutional Review Board at Brooke Army Medical Center, Ft. Sam Houston, TX, and the U.S. Army Human Subject Research Review Board, Ft. Detrick, MD.

Resting Protocol (Healthy Subjects)

Healthy subjects in both the resting and lower body negative pressure (LBNP; described below) protocols maintained their normal sleep pattern, refrained from exercise, abstained from caffeine and other autonomic stimulants for at least 24 h prior to the experiment, and underwent a brief medical examination. Each subject gave written informed voluntary consent prior to participation. There were 20 healthy, nonsmoking subjects (14 men/6 women; 30 ± 2 yr) who were instrumented with a lead II ECG to record R-to-R intervals (RRI). These subjects then rested in the supine position for at least 10 min while an ECG was continuously recorded.

LBNP Protocol (Healthy Subjects)

There were 108 healthy, nonsmoking subjects (63 men/45 women; 28 ± 1 yr) who participated (including the 20 subjects from the resting protocol). All subjects were instrumented with a lead II ECG. LBNP was used as an experimental tool to simulate loss of central blood volume (5). Briefly, with the supine subject sealed into a vacuum chamber at the waist, application of negative pressure to the lower body results in a redistribution of blood from the upper body to the lower extremities and abdomen. Following a 5-min baseline, resting period without LBNP, each subject underwent exposure to a progressive LBNP protocol designed to test their tolerance to experimentally induced central hypovolemia (5). The LBNP protocol consisted of 5 min of chamber decompression at −15, −30, −45, and −60 mmHg and then additional increments of −10 mmHg every 5 min until the onset of hemodynamic decompensation or the completion of 5 min at −100 mmHg. Hemodynamic decompensation was defined as either a precipitous fall in systolic blood pressure, the onset of presyncopal symptoms such as gray-out, sweating, nausea, or dizziness, or a combination of decreasing blood pressure with symptoms. Upon hemodynamic decompensation, the pressure within the chamber was immediately returned to 0 mmHg and the subjects were monitored for 10 min (recovery period).

Trauma Patient Protocol

ECGs were obtained from trauma patients transported by helicopter from the injury scene to Level I trauma centers (5). From 2988 patient records stored in the Trauma Vitals database system (5), the records of 700 patients monitored using a PIC50 defibrillator/vital signs monitor (Welch Allyn, Buffalo Grove, IL) during air transport were selected. For the purpose of a separate study, we selected patient records based on the presentation of normal vital signs in the pre-hospital setting, including: 1) systolic blood pressure greater than or equal to 90 mmHg; 2) motor Glasgow Coma Score of 6; 3) normal radial pulse (on a scale of absent, weak, or normal, as identified by emergency medical personnel); and 4) normal capillary refill. This down-selection resulted in a set of 245 patient records (166 men/79 women; 38 ± 1 yr).

Data Analysis

ECG waveforms were analyzed with a commercially available software analysis package (WinCPRS, Absolute Aliens, Turku, Finland). Each ECG waveform was manually scanned for the presence of electromechanical noise or EBs. An EB was defined as an RRI that was < 80% or > 120% of the previous RRI value (9); by definition, this included EBs of both atrial and ventricular origins. For healthy resting subjects, the final 800 RRI segment of the ECG recording was used for analysis. For subjects exposed to LBNP, the entire ECG waveform from the LBNP experiment (2331 ± 34 s, range 1657–3100 s) was used. Finally, for the trauma patients, the first 800 RRI segment that was relatively clean of noise was used for analysis. Chi-square (χ^2) analysis was used to test whether the frequency of EBs was independent of population (resting subjects, LBNP subjects, trauma patients).

In 15 of the trauma patients, the 800 RRI ECG segment contained only 1 EB. To ascertain the effect of just 1 EB on the calculation of some common heart period variability metrics, the 800 RRI segment was analyzed both with and without linear interpolation of the EB. Filtered and cleaned ECG signals were analyzed with a commercially available software program (WinCPRS, Absolute Aliens, Turku, Finland). Heart period variability was assessed in the time domain using the standard deviation of average RRI, the square root of the mean squared differences of successive RRIs, and the percentage of adjacent normal RRIs that varied by at least 50 ms or more (pNN50). To assess heart period variability in the frequency domain, consecutive RRIs were first replotted using linear interpolation, resampled at 5 Hz, and then passed through a low-pass impulse response filter with a cutoff frequency of 0.5 Hz. After passing data sets through a fast Fourier transform with a Hanning window (6,7), heart period variability was quantified by calculating the power spectral density in high frequency (0.15-0.4 Hz) and low frequency (0.04-0.15 Hz) bands. Finally, sample entropy and fractality (fractal dimensions by curve length; FD-L) were calculated as representative metrics describing the nonlinear characteristics of the RRI segment (13). Briefly, sample entropy measures the complexity of signals, with values decreasing as the signal becomes less complex and more regular (13). FD-L characterizes the fractal dimension of the signal curve, which is an indication of the self-similarity of the signal; low values indicate low levels of fractality or self-similarity, while high values indicate high levels of fractality and increased complexity (1,13). For each of these metrics, the effect of the EB in each segment was

quantified by calculating the percentage difference between the interpolated and non-interpolated values.

RESULTS

ECG waveforms from 4 of the 20 (20%) resting healthy human subjects contained at least 1 EB (**Fig. 1**). Of these four subjects, two ECG records contained one EB, one contained four EBs, and one contained five EBs. Similarly, at least one EB was found in 17.6% of the healthy subjects undergoing LBNP. Because these records were obtained under laboratory conditions, there was no evidence of electromechanical noise.

In the 245 ECG waveforms from trauma patients, 117 waveforms were found to contain: 1) EBs (85 waveforms; 34.7%); 2) electromechanical noise (3 waveforms; 1.2%); or 3) < 800 heartbeats (29 waveforms; 11.8% of total). EBs were more prevalent in trauma patients than in healthy subjects either during rest or LBNP (χ^2 = 11.48, P = 0.003).

Table I illustrates the effects of even 1 EB within an 800 RRI segment on several common heart period variability metrics. The presence of a non-interpolated EB changes the values of these variables by up to 41% on average, with the time and frequency domain metrics being particularly sensitive to the EB. Importantly, the ranges of the EB effect indicate significant individual variability, with some metrics changing by up to 400% in some individuals.

DISCUSSION

As hypothesized, a greater percentage of ECG waveforms from our trauma patient population contained EBs than those acquired from healthy human subjects, either at rest or during experimentally induced central hypovolemia. In two additional studies using ECG waveforms from pre-hospital trauma patients, the incidence of EBs was similarly high at 28% (4) and 40% (1) (**Fig. 2**) and these patients were subsequently excluded from analysis. Furthermore, a study by Cooke et al. ex-

TABLE I. EFFECT (% DIFFERENCE) OF 1 EB IN AN 800 RRI ECG SEGMENT ON SOME COMMON HEART PERIOD VARIABILITY METRICS.

Metric	Difference, %	Range
Time Domain		
RRISD, ms	3.2 ± 1.6	0–22
RMSSD, ms	26.0 ± 10.3	0–125
pNN50, %	40.5 ± 30.9	0–400
Frequency Domain		
HF, ms^2	37.6 ± 15.7	0–200
LF, ms^2	0.5 ± 0.7	−6.3–5.3
HF/LF	37.7 ± 16.3	0–200
Nonlinear		
Sample Entropy	-2.2 ± 0.9	−11.5–0
Fractality (FD-L)	0.39 ± 0.16	−0.05–2.25

ECG records are from trauma patients in the pre-hospital setting. Data are means $\pm$ SE ($N = 15$) and ranges of individual differences. RRISD, standard deviation of average RRI; RMSSD, square root of the mean squared differences of successive RRIs; pNN50, percentage of adjacent normal RRIs that varied by at least 50 s; HF, power spectral density in the high frequency band (0.15-0.4 Hz); LF, power spectral density in the low frequency band (0.04-0.15 Hz); FD-L, fractal dimensions by curve length.

cluded 11 of 26 patients (42%) from further analysis due to noise and/or EBs in the ECG signal (6). Taken together, these data suggest that trauma patients are more likely to exhibit aberrant beats than healthy humans. Excluding such a large percentage of patients from analysis incurs a high risk of selection bias (20) and challenges the practical utility of these metrics in the clinical setting.

A number of studies have shown that EBs can interfere with heart period variability calculations and can subsequently result in erroneous values (20). Generally, a higher incidence of EBs is associated with a higher heart rate (21), which is common in trauma patients due to injury, pain, and/or anxiety. In addition to tachycardia, the presence of alcohol, caffeine, illicit drugs, or sleep deprivation may also increase the likelihood of EBs (14,19); each of these physiological states is
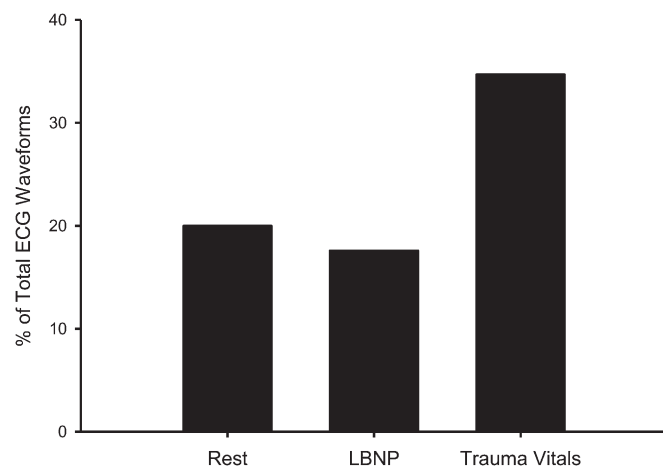
Fig. 1. The percentage of total ECG waveforms containing ectopic beats in healthy resting humans (Rest, $N = 20$), healthy humans undergoing lower body negative pressure (LBNP, $N = 108$), and in trauma patients (Trauma Vitals, $N = 245$).
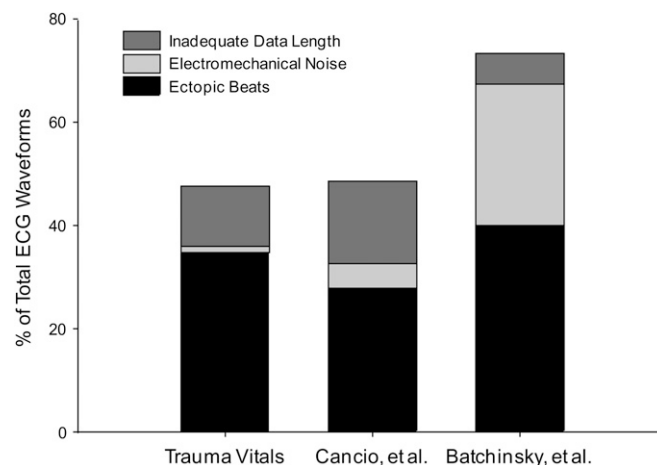

Fig. 2. The percentage of total ECG waveforms from trauma patients excluded from further analysis in this study (Trauma Vitals) and in previously published papers by Cancio et al. (4) and Batchinsky et al. (1).

commonly observed in trauma patients, with the incidence of detectable alcohol in the blood being as high as 47% in emergency room trauma admissions (17). If a patient is deteriorating but exhibits a high number of EBs, these irregular RRIs may falsely increase heart period variability values when, in fact, heart period variability should be decreasing. It is, therefore, highly recommended that ECG data containing EBs should not be considered for use in data analysis and/or patient diagnosis (3,20). In fact, in this study, the presence of only one EB produced significant (up to 400%) alterations of some heart period variability metrics in individual patients (Table I). These results confirm the profound influence of simulated EBs and other artifacts on time- and frequency-domain metrics observed in a previous systematic investigation of this issue (3). The data contained within Table I also offer the first indication that the nonlinear metrics characterizing the level of complexity contained within the ECG signal (i.e., sample entropy and fractality) may be less affected by the presence of a single EB than the linear time and frequency domain metrics.

Similarly, if the ECG signal contains electromagnetic noise or limited continuous RRIs, many heart period variability metrics cannot be accurately calculated (20) and waiting for noise-free and EB-free intervals may not be appropriate when clinical management decisions need to be made quickly. Importantly, based on our analysis, these limitations potentially exclude between ~48–74% of pre-hospital trauma patients (Fig. 2) or, on an individual basis, heart period variability assessments could only be applied to ~26–52% of patients. These limitations may also apply to the more controlled in-hospital setting, as evidenced by the exclusion of 52% of patients monitored in an ICU during burn resuscitation from analysis of heart period variability (2). Without advanced analyses to overcome these limitations (e.g., development of filtering techniques or use of metrics insensitive to EBs or noise), the practical utility of heart period variability for monitoring these patients is questionable. Alternatively, it is possible that the increased incidence of ectopy itself could be used as a diagnostic tool (e.g., heart rate turbulence; 18).

Although heart period variability metrics have initially shown promise in indicating the requirement for life saving interventions and survival from injury in trauma patients, results from this study and others indicate that this patient population in particular exhibits a relatively high level of EBs. Because accurate determination of heart period variability metrics is not currently possible in the presence of EBs, application of heart period variability metrics to monitoring trauma patients in the pre-hospital setting is therefore problematic as this patient population characteristically displays a substantial reduction in eligible ECG waveforms. Implementation of this monitoring tool for unstable patients in the pre-hospital setting must, therefore, be cautioned as its proper application cannot be realized in a majority of patients.

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